



March 28, 2011

Dr. Angela Nugent, Designated Federal Officer
EPA Science Advisory Board (1400R)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW.
Washington, DC 20460

Dear Dr. Nugent:

The American Chemistry Council (ACC) appreciates this opportunity to provide comments to the EPA's Science Advisory Board Committee on its draft findings in the report entitled "Draft - Science Integration for Decision Making"¹ (SAB Draft Report). ACC² has long maintained that the practice of federal agency risk assessment can and should reflect the best science and practices in risk assessment, and we support actions to enhance the integration of up to date scientific knowledge, methods and practices in risk assessment and decision making programs across EPA. Advancing the technical quality and objectivity of EPA risk assessments, particularly by promoting more transparency in what science is being considered and how it is being interpreted, and integrating this within program office decision-making practices, will go a long way to assuring that potential risks are objectively portrayed and thus improving decision making.

As the SAB Draft Report illustrates, it is not enough simply to have the science available for use. There must be both a structural means and a willingness within EPA programs to enable integration of the science into policies, procedures and practices. Assuring the quality, objectivity, utility, transparency and integrity of risk assessment practices across EPA and particularly within EPA's IRIS program, and integrating this into decision making, are shared objectives. ACC's specific comments are attached. Please do not hesitate to contact me concerning any aspect of these comments.

Sincerely,

Richard A. Becker, Ph.D., DABT
Regulatory and Technical Affairs Department

¹ 03/11/11– Draft report "Science Integration for Decision Making"

[http://yosemite.epa.gov/sab/sabproduct.nsf/ea5d9a9b55cc319285256cbd005a472e/b7a1ea67f365a21785257850007d6644/\\$FILE/SciIntegDecMaking-Rept--03.11.11.pdf](http://yosemite.epa.gov/sab/sabproduct.nsf/ea5d9a9b55cc319285256cbd005a472e/b7a1ea67f365a21785257850007d6644/$FILE/SciIntegDecMaking-Rept--03.11.11.pdf)

² The American Chemistry Council (ACC) represents the leading companies engaged in the business of chemistry. ACC members apply the science of chemistry to make innovative products and services that make people's lives better, healthier and safer. ACC is committed to improved environmental, health and safety performance through Responsible Care®, common sense advocacy designed to address major public policy issues, and health and environmental research and product testing. The business of chemistry is a \$674 billion enterprise and a key element of the nation's economy. It is one of the nation's largest exporters, accounting for ten cents out of every dollar in U.S. exports. Chemistry companies are among the largest investors in research and development. Safety and security have always been primary concerns of ACC members, and they have intensified their efforts, working closely with government agencies to improve security and to defend against any threat to the nation's critical infrastructure.



**American Chemistry Council Comments on
EPA's Science Advisory Board's
"Draft Report: Science Integration for Decision Making (3/11/2011)"**

1. Introduction

The SAB Science Integration for Decision Making Committee's review is both timely and important. As the draft report illustrates, it is not enough simply to have the science available for use. There must be both a structural means and a willingness within EPA programs to enable integration of the science into policies, procedures and practices. In the draft report, the Committee identifies areas where there has been good use of science and integration of science as well as areas requiring improvement. Notably, the Agency programs associated with successful science integration and decision making have embraced robust problem formulation early on in the assessment process as well as input from the broader scientific community, including stakeholders. The SAB Draft Report notes (page 25): "Openness and transparency is a common theme as managers discussed science assessment practices that have benefited individual decisions and strengthened their organizations." Examples taken from the SAB Draft Report where the Committee reports successful integration of science and decision making include:

- *ORD's National Center for Environmental Assessment and Ecosystem Research Program, for example, have formed Agency work groups, and coordinated across federal agencies and with outside scientists to frame problems related to biofuels, climate change.... (pg. 16)*
- *...the Office of Transportation and Air Quality seeks science and engineering information from the Health Effects Institute, an independent non-profit research organization funded primarily by EPA and the motor vehicle industry and from stakeholders, such as automobile companies who can both contribute to and challenge EPA's analysis. (pg. 20).*
- *Similarly, OSWER...turns to the Department of Defense, the Department of Energy, the National Aeronautics and Space Administration, Argonne National Laboratories, and U.S. Army Corps of Engineers for the science it needs for treatment and site-characterization decisions...(pg. 21)*
- *Compared to many EPA science assessments, NAAQS reviews are more transparent; they allow for multiple opportunities for public comment and for peer review by the Clean Air Scientific Advisory Committee, a federal advisory committee dedicated to providing review and advice for the NAAQS (pg. 24).*

The common thread present in these examples of success is the broader role and involvement of scientific input from outside of the EPA at various points throughout the assessment from the initial problem formulation stage, through the assessment, peer review and final stages all take advantage of this external scientific input.



In the SAB Draft Report, the Committee also describes programs /areas where Agency science integration with decision making falls short, and where improvement is needed. There is a general recognition that one of the areas needing greater attention is the IRIS program. IRIS is repeatedly mentioned in the report as a program that needs strengthening. We believe that IRIS – and those who use that system – would benefit from more effective integration of science to assure that the most up-to-date, reliable, and high quality scientific analyses are used. As noted (page 26) of the SAB Draft Report:

EPA regions and many programs voiced consensus that EPA's needs for IRIS assessments outstripped ORD's capacity for timely production IRIS values. Interviewees identified several major issues.... They observed that the IRIS process was lengthy and that stakeholder challenges can lead to delays in completing IRIS assessments because "arguments about how to interpret the available science are perpetuated to keep new science from being implemented." Simultaneously, new risk assessment approaches, such as EPA's 2005 Cancer Guidelines, calls for increasingly high quality, nuanced science assessments, which no longer default to linear low-dose extrapolation for cancer or assume that a cancer value trumps all other effects. With all the focus on and expectations for IRIS, many managers voiced concern that EPA lacked a reliable schedule for generating IRIS assessments on which the whole Agency could depend.

ACC believes that there are several recommendations that the SAB should consider offering that would go a long way to enhance the quality and productivity of the IRIS assessments prepared by ORD. ACC believes that those recommendations should start with the Framework put forward in the SAB Draft Report (page 5) describing some of the necessary steps to achieve full science integration, specifically, Problem Formulation, Acquisition of the Science Required, Assessment of Available Science, and Integration of available science across different disciplines and sources.

2. Problem Formulation and Acquisition of the Science Required

Greater and more effective science integration for decision making within the IRIS program would occur if the program made better use of scientific methods and analyses from other EPA programs, other Federal programs and from scientists from the public and private sectors. With respect to integrating science from other EPA and Federal programs, the IRIS program has not made use of readily available opportunities to more rapidly develop new assessments, or revise out-dated assessments. For example, the program has not systematically used recent scientifically robust, peer reviewed, chemical risk assessments developed by, or for, other EPA and Federal Agency programs and authoritative scientific organizations as starting points for new or updated IRIS assessments. The risk assessments prepared for the EPA's Voluntary Children's Chemical Evaluation Program (VCCEP) are examples of up-to-date, scientifically rigorous risk assessments that the IRIS could integrate into their program.³ The use of such assessments (or similar high-quality assessments developed by other federal agencies or comprehensive risk assessments authored outside government that have undergone independent scientific review for transparency, completeness and quality) should result in more rapid and IRIS assessments without compromising scientific quality. Of course, EPA would need to develop a process for evaluating

³ See <http://www.tera.org/peer/VCCEP/Chemicals&Schedule.html> for background information, to access the assessments and to read the findings of the peer consultation panel reviews.



the scientific quality of such assessments to assure they comply with its own standards, as well as develop a means for appropriate revision. The IRIS program's use of such comprehensive and scientifically rigorous assessments as the initial step in an IRIS assessment or an IRIS update would provide considerable savings in resources, time and effort by EPA and would increase throughput in the program.

Over the last 10-15 years, the IRIS assessments have required greater scientific effort and time to prepare because the science of risk assessment has advanced and the techniques and approaches applied 20 years ago are now outdated. New scientific methods must now be used in IRIS assessments. These methods include the development and application of modeling for dose extrapolation across species and routes of exposures, incorporation of biologically based modes of action, explicit evaluation of possible differential sensitivity at different life stages and use of chemical specific adjustment factors. It must be emphasized that there is a need to have IRIS fully evaluate the best available scientific data. Currently, many assessments require several time consuming iterations to achieve the necessary degree of comprehensiveness and objectivity. ACC suggests that it may be possible to overcome such limitations if EPA were to initiate a problem formulation process early on in the IRIS sequence. The IRIS Office should undertake an initial review of the available data on a chemical to be reviewed in order to identify the perceived issues/concerns anticipated in preparing the assessment. The initial review should be based on a preliminary review of the available data and should seek to identify: 1) key science issues that could benefit from supplemental information/data generation; 2) issues likely to be considered controversial among stakeholders; and 3) analyses that could be performed within the short-term that might provide greater clarity on science issues that will need to be addressed.

In 2006, the Government Accountability Office (GAO) issued its report entitled Human Health Risk Assessment -- EPA Has Taken Steps to Strengthen Its Process, but Improvements Needed in Planning, Data Development, and Training.⁴ In that report the GAO's recommendations included, that 1) EPA enhance early planning of each risk assessment; and 2) EPA identify and communicate data needs to the public and private research community. Developing a literature search and requesting any additional information is a step in the right direction to help promote EPA's integration of science coming into the Agency from outside sources. However, additional enhancement – by engaging stakeholders in a dialogue on the problem formulation can help ensure that risk assessments are based on the best available information and are appropriately scaled and oriented to the relevant questions. These process improvements allow the Agency to identify and then collect scientific information on possible modes of action at the right time in the process (at the literature search/request for data stage), so that these can be explored, evaluated, and if appropriate, used in the quantitative stage of the risk assessment.

If data needs⁵ are identified during the Problem Formulation stage, then a process should be established to develop any needed information. EPA may elect to require data to be generated pursuant to

⁴ Available at <http://www.gao.gov/new.items/d06595.pdf>.

⁵ A hazard based “data gap” is not necessarily a “data need” with respect to characterizing potential risks. A “data gap” indicates information that is lacking, and can refer to data, analyses or presentation; not every “data gap”, however, is a “data need.” “Data needs” are those specific “data gaps” requiring additional work before the potential risks can be adequately characterized. Devoting resources to toxicity “data gaps” irrespective of whether the specific information is actually needed (that is, data or information which is viewed as necessary to characterize risks with an adequate degree of scientific certainty), would be scientifically unjustifiable, require unnecessary animal testing and unwarranted costs. For further discussion in the context of a chemical assessment see TERA (page 19)



the Agency's data generation authorities, although in most circumstances, it may be adequate to provide the affected industry with a description of the data that would be needed for a comprehensive assessment. By describing the rationale for the data, EPA will be able to explain to stakeholders how the supplemental information would improve the science basis of the assessment, reduce uncertainty and enable the Agency to formulate a more accurate assessment.

While this might require some additional time and effort at the initial stages to properly formulate the problem and design the assessment accordingly, this will be time and effort well invested. Such a problem formulation process could closely follow the release of the literature review. Stakeholder engagement at this stage will assist EPA in identifying the key issues that the IRIS assessment must address. As the NRC Science and Decisions⁶ panel has recommended, this "should result in concrete outputs detailing the rationale and findings of the early design process." The upfront investment should lead to a more complete, high quality initial draft assessment that is "fit for purpose." And this should be expected to reduce the time and effort that is needed for re-analysis and re-drafting when a poor, "not fit for purpose" draft assessment is developed. More attention to problem formulation should also assist EPA in developing a realistic and reliable schedule for conducting the assessment. We strongly recommend, therefore, that IRIS change and implement an upfront problem step that willingly accepts and acts upon input from other EPA offices, other Federal Agencies and the public stakeholders. These improvements should contribute to more transparent and scientifically comprehensive and robust IRIS assessments that reflect the most up-to-date scientific research and knowledge.

3. Assessment and Integration of Available Science

To better integrate scientific methods across EPA also requires consideration of ways to enhance the manner in which EPA engages with the broader scientific community. EPA can increase peer involvement by both organizing and participating in venues that encourage the open exchange of data, insights, and ideas from scientific experts across the academic, public and private sectors. For this to be successful EPA scientists should be encouraged to participate in multi-sector forums focused on improving the design, conduct, interpretation and communication of health and environmental risk assessments. EPA does not have a monopoly on risk assessment science and procedures. It is imperative that EPA engage not only in Agency-sponsored activities, but also multi-sector forums, where there is open and frank exchange and discussion of methods, scientific data and analyses developed in academia, in research institutes and in both the public and private sectors.

Over the last 35 years, toxicology has evolved from a largely observational discipline to what is today a discipline that applies advanced scientific techniques and knowledge to investigate how chemicals interact with biological systems, at the molecular, cellular, organ and organism levels, in order to understand the biological basis for the induction of toxicity. Research programs within industry, academia and government labs have greatly expanded to investigate the underlying biological mechanisms and modes of action of toxicants. A goal has been to apply this knowledge to improve the scientific basis of government regulatory policies and industry product stewardship. However, many challenges have been encountered in translating up-to-date scientific knowledge of how chemicals act at the molecular, cellular and organ level to assessing potential human health risks and integrating this into decision making.

⁶ Science and Decisions: Advancing Risk Assessment (2009). National Research Council, Washington, DC. Page 67



Today, as a consequence of continued rapid advances in scientific understanding and the application of this understanding to regulatory science policy, decision logic for evaluating the biological events leading to toxicity and consideration of how these events relate to human risk is possible as a routine matter in risk assessment. Significant progress has been made, both in the U.S. and internationally, in defining rigorous scientific frameworks for evaluating toxicity datasets to determine biologically plausible modes of action and to determine relevance to humans. In practice, however, movement away from default assumptions has been slow to develop, particularly in the IRIS program, despite significant investments by government, academia and industry into toxicological research. Failure to recognize and act on advances in scientific knowledge and the best available, most relevant scientific data in conducting IRIS assessments and integrating this into program decision making wastes investments in research and undermines development of new science-based risk assessment practices and effective public health science policy. Indeed, that approach essentially freezes in time past practices and limits the application of scientific advances to a foundation based on outdated understandings of the science.

To enhance the integration of science into the IRIS program, ACC recommends that IRIS should employ, and document the application of, objective criteria for determining method validity, data quality and study reliability. We also recommend when mode of action analysis has been identified at the problem formulation stage, the Agency should use a structured evaluative framework, such as that of the World Health Organization International Programme on Chemical Safety “Mode of Action Framework”⁷ or the ILSI “Key Events Dose Response Framework,”⁸ to provide a systematic approach for assessing the overall weight of the evidence for observed effects and the postulated mode(s) of action.

To provide an objective and fully transparent analysis, EPA should consider conducting a hypothesis based weight of evidence analysis, where the default mode of action is assessed side-by-side with the postulated biologically plausible mode(s) of action. Such an approach will enhance integration of science into the IRIS assessment by improving the understanding of the extent to which the available data support the postulated mode of action instead of the default and vice versa. In this manner data from laboratory experiments, epidemiological investigations, and cutting-edge mechanistic research from all relevant studies—GLP and non-GLP—and from all investigators, regardless of affiliation or funding source, can be comprehensively reviewed, given appropriate weight, and integrated in a manner that provides a robust understanding of the potential hazards and risks that exposures to a substance could pose.

Independent External Peer Review Is a Critical Step in Promoting Quality Science Integration

Independent external peer review is also a critical step to ensure the development of high caliber IRIS assessments and is an important conduit in the process for science integration into decision making. Peer review is defined by EPA as “an in-depth assessment of the assumptions, calculations, extrapolations, alternate interpretations, methodology, acceptance criteria, and conclusions pertaining to

⁷ http://www.who.int/ipcs/methods/harmonization/areas/cancer_mode.pdf

⁸ E. Julien et.al. (2009). The Key Events Dose-Response Framework: A Cross-Disciplinary Mode-of-Action Based Approach to Examining Dose-Response and Thresholds. *Critical Reviews in Food Science and Nutrition*, 49: 8, 682 — 689.
http://pdfserve.informaworld.com/894199__914014390.pdf



the specific major scientific and/or technical work product and of the documentation that supports them.”⁹ Peer review plays a crucial role in development of the best scientific evaluation and is integral to identifying information that would reduce uncertainty in significant areas of the assessment. The process of peer review should be structured to accomplish these objectives. There are several areas to consider for enhancing the IRIS peer review process:

- Rather than base Peer Review Charge Questions solely on the input provided by the lead Agency Office, the preparation of these Charge Questions should reflect stakeholder input and be developed using an iterative process. Development of the Charge Questions should be initiated at the Problem Formulation step, and then issued as a refined draft coinciding with the release of the draft IRIS assessment. Public comments on this draft of Charge Questions should be solicited.
- The peer review Charge Questions should be written in order to facilitate objective consideration of alternative plausible scientific views rather than from the vantage point of giving deference to the interpretation presented in the draft IRIS assessment. This provides the Peer Reviewers greater opportunity to consider alternative scientific views such as those sometimes offered by stakeholders.
- As recommended in “Improving the Use of Science in Regulatory Policy,” EPA should “explicitly differentiate between questions that involve scientific judgments and questions that involve judgments about economics, ethics and other matters of policy.”¹⁰
- There needs to be improvement so that public comments are meaningfully and fully considered. ACC recommends the IRIS program consider ways to revamp the Listening Session in a manner that promotes open and frank discussions by EPA with stakeholders on the key scientific issues and analyses. Discussion of the Charge Questions is an activity that EPA should consider including in such a revised Listening Session.
- The Peer Review meetings should be restructured to encourage open scientific dialogue and thoughtful scientific deliberation. Stakeholder input should not be limited to a few minutes at the beginning of a meeting; greater effort should be made to structure the meetings so that stakeholder input is provided and deliberated at strategic times throughout the meeting. Moreover, Peer Reviewers should not be dissuaded from embarking on open technical discussion/scientific exchange with stakeholders. Overall, a much more open process should be promoted.
- In selecting peer review panel members, the foremost consideration should be given to expertise. Qualified scientists from industry should be given equal consideration for appointment based on the subject matter, and in accordance with applicable conflict of interest provisions. In this there is unanimity among the most authoritative sources, including the National Academies of Science and the Society of Toxicology: “Appointments to scientific advisory bodies should be based principally on the scientific credentials, demonstrated accomplishments, and professional

⁹ EPA Peer Review Handbook 3rd Edition. Page 12 http://www.epa.gov/peerreview/pdfs/peer_review_handbook_2006.pdf

¹⁰ Shortly after her confirmation, EPA Administrator Jackson declared “policy decisions should not be disguised as scientific findings.” The Bipartisan Policy Commission’s report “Improving the Use of Science in Regulatory Policy” makes the same recommendation. <http://www.bipartisanpolicy.org/sites/default/files/BPC%20Science%20Report%20fnl.pdf>



credibility of the nominee. His/her source of employment and funding (past or present), religious beliefs, political persuasion, sexual orientation, gender, or race/ethnicity should not be used as (a) determinant(s) of exclusion to such a scientific advisory body.”¹¹

4. Conclusions

As the SAB Draft Report illustrates, it is not enough to have the science available for use. There must be both a structural means and a willingness within EPA programs to enable integration of the science into policies, procedures and practices. Assuring the quality, objectivity, utility, transparency and integrity of risk assessment practices across EPA and particularly within EPA’s IRIS program, and integrating this into decision making, are shared objectives. Time-consuming and resource-intensive disputes could be avoided, and defensible health-based reference doses and standards could be issued more quickly and at lower cost, by improving the policies and practices within EPA’s risk assessment programs. Such improvements in the IRIS Program should include requiring:

- 1) A formal “problem formulation” step that includes open discussions with stakeholders (EPA offices, other agencies, stakeholders, etc.) concerning the needs and objectives, key areas for the design and conduct of the assessment, the types of analyses needed for a high quality assessment (approaches based on default assumptions and those based on data) given the existing data and planned or ongoing research;
- 2) Application of a systematic framework for evaluating weight of evidence that entails quantitative assessment of biologically plausible modes of action in lieu of, or at the very least in addition to, default assumptions;
- 3) Robust scientific peer review, which includes appropriately formulated charge questions (taking into consideration stakeholder input and comments), and fully responsive and timely Agency actions in addressing the peer review findings and recommendations; and
- 4) Transparency in all aspects of the assessment, including documenting full consideration and the rationale for action or inaction with respect to comments received on key substantive scientific issues.

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ACC appreciates the opportunity to submit these comments. For more information, or clarification, on any of the points raised please contact Richard A. Becker, Ph.D., DABT at 202-249-6405 or by e-mail at Rick_Becker@americanchemistry.com.

¹¹ Society of Toxicology, “Appointment and Participation of Scientists on Peer Review Panels and Scientific Advisory Boards” <http://www.toxicology.org/pm/AdvisoryBoard.asp>

